Supplemental Material



Figure S1. Modeled structure and electrostatic potential surface of murine Nav 1.5 channel with phosphatidylinositol-3, 4, 5-triphosphate (PIP3). A. Modeled structure of murine Nav 1.5 channel with PIP₃ (top view). **B**. Modeled electrostatic potential surface of murine Nav 1.5 channel with PIP₃.



Figure S2. **Structure and domain architecture of modeled human Nav 1.5 channel**. **A**. Modeled structure of human Nav 1.5 channel. **B**. Domain architecture of modeled human Nav 1.5 channel.



Figure S3. Phosphatidylinositol-3, 4, 5-triphosphate (PIP₃) interaction with human Nav 1.5. A. Top and side view of human Na_V 1.5 channel with PIP₃. B. Electrostatic potential surface of the human Na_V 1.5 channel (top view) with PIP₃. C. Region of human Na_V 1.5 channel interacting with PIP₃. Gln, glutamine; Lys, lysine; Thr, threonine.

Supplemental Video Legends:

Video S1. **Wild-type (WT) heart at baseline**. Pseudo-color video of epicardial imaging with voltage sensitive dye RH237. The 2-s recording of the post-stimulation interval at 50 frames/s. Acquisition frame rate 1,000 frames/s. Best viewed with Windows Media Player.

Video S2. **Wild-type (WT) heart at 1-min reperfusion**. Pseudo-color video of epicardial imaging with voltage sensitive dye RH237. The 2-s recording of the post-stimulation interval at 50 frames/s. Acquisition frame rate 1,000 frames/s. Best viewed with Windows Media Player.

Video S3. p110 α **-DN** (constituent PI3K α -deficient) heart at baseline. Pseudo-color video of epicardial imaging with voltage sensitive dye RH237. The 2-s recording of the post-stimulation interval at 50 frames/s. Acquisition frame rate 1,000 frames/s. Best viewed with Windows Media Player.

Video S4. p110α-DN (constituent PI3Kα-deficient) heart at 1-min reperfusion. Pseudo-color video of epicardial imaging with voltage sensitive dye RH237. The 2-s recording of the post-stimulation interval at 50 frames/s. Acquisition frame rate 1,000 frames/s. Best viewed with Windows Media Player.